REMARKS

Claim 1 is pending in this application. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. 102

Claim 1 has been rejected under 35 U.S.C. 102(a) as being anticipated by Chamberlain et al. (1998). The Examiner suggests that this reference teaches administration of methotrexate to patients with leptomeningeal metastases presenting with radiculopathy, wherein the dose of methotrexate is administered intraventricularly and is a dose of 2 mg daily (total dose of 40 mg). The Examiner suggests that because Chamberlain et al. teach the same composition of methotrexate in the same dose (less than 3 mg/kg) to be useful in the treatment of leptomeningeal metastases with radiculopathy, that methotrexate would inherently be treating the radiculopathy, whether explicitly recognized or not. Further, the Examiner suggests that the administration of methotrexate intraventricularly overlaps with the administration route of the invention as claimed, such that Chamberlain et al. anticipates the claimed invention. Applicants respectfully disagree with the Examiner's conclusions regarding this reference.

As presented in the response dated July 6, 2005, which was entered as a preliminary amendment upon filing the Request for Continued Examination (RCE), claim 1 has been amended to recite that local administration into the back of the animal is intrathecal administration, as is defined in the specification as filed at page 5, and acknowledged by the Examiner.

Also as discussed in the previous response, Chamberlain et al. (1998) disclose only the intraventricular administration of

methotrexate, the route that is discussed by the Examiner. The Examiner is mistaken in the assertion that intraventricular administration of a drug is the same as intrathecal administration. It is general principle of human physiology and pharmacokinetics that intraventricular administration will not produce a local concentration of active drug in the spinal cord area that is anywhere near the same concentration as would be achieved with intrathecal administration. This is because, as taught in basic human anatomy and physiology texts (e.g., *Human Anatomy and Physiology*, Second Edition, Elaine N. Marieb (editor), Benjamin Cummings Publishing: Redwood City, CA, pages 404-405, starting at the second column on page 404 provided with the response filed July 6, 2005) the circulation of cerebrospinal fluid through the brain ventricles is designed such that only some of the cerebrospinal fluid from the ventricles circulates into the central canal of the spinal cord. As is taught in this text, "most enters the subarachnoid space" (see page 404, second column, line 3-4 of second paragraph). Therefore, since intraventricular injection of methotrexate as taught by Chamberlain et al. (1998) would result in only a small amount of circulation of the injected drug, via the cerebrospinal fluid, into the spinal cord, the concentration of methotrexate achieved would not be expected by one of skill in the art to be as high as could be achieved through direct administration into the spinal cord area via intrathecal administration. The subarachnoid space, as shown in Figure 12.20 on page 404 of the text cited above, is not the area touched through intrathecal administration. Thus, this fact, combined with the fact that nowhere does the cited reference teach or suggest use of methotrexate intrathecally at any dose for relief of pain

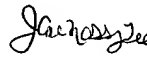
indicates that this reference does not teach or suggest the method of the instant invention. It is critical to understand that the concentration of drug achieved at the local site, in the spinal cord, must be high enough to produce a pharmacological effect, without producing unwanted side effects. This is another basic tenet of pharmacology; dose-response dictates whether a drug is effective and safe. Such a pharmacological action, with safety, is only achieved by intrathecally administering the drug, NOT by giving the drug into the brain's ventricular system as the Examiner suggests.

In order to anticipate an invention, the cited reference must teach each and every limitation of the claims (MPEP 2131). Accordingly, this reference cannot anticipate the claims as amended. Withdrawal of this rejection is respectfully requested.

II. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



Jane Massey Licata
Registration No. 32,257

Date: **November 15, 2005**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053
856-810-1515